THE BRITISH JOURNAL OF
VENEREAL DISEASES

SEPTEMBER 1945 VOL. XXI NO. 3

THE CUTANEOUS MANIFESTATIONS OF GONORRHOEA*

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Skin manifestations seen in association with gonorrhoea may or may not harbour the gonococcus. Lesions due to the gonococcus usually occur locally in the region of the primary focus of infection but they may also be systemic in origin. The most distinctive skin eruption is keratodermia blennorrhagica, which also occurs, although rarely, in cases in which there is no history of gonorrhoea; evidence is brought forward that it is due to a virus.

There are also conditions, such as gonococcal infections of para-urethral ducts and glands which open on the skin or mucous membrane of the urogenital tract, which may simulate gonococcal ulcers. An abscess of the prostate, Cowper's glands, or inguinal glands (including suppurative lymphangitis), or a peri-urethral abscess, may also discharge its gonococcal contents through the skin. When an abscess of the prostate or of Cowper's gland occurs in the perineum the skin is red and inflamed, and (before the abscess bursts spontaneously or is drained) the area may be mistaken for primary gonococcal involvement of the skin and subcutaneous tissues. Scholtz does, however, describe a case of primary gonococcal cellulitis of the perineum in which there was no involvement of the deeper structures.

Venereal warts (condylomata acuminata), due to a virus which can only be demonstrated by inoculation experiments, are also seen in association with gonorrhoea.

Since the introduction of the sulphonamides and of penicillin all skin lesions have become extremely rare; they now occur only in a small percentage of cases showing drug resistance or in cases which have received no treatment.

Local lesions: genital and extragenital

In my experience local lesions are always situated in the skin or mucous membrane of the genital regions, but extragenital ulceration not associated with systemic infections has been reported quite frequently in the literature. The lesions are usually in association with gonococcal infections of the urogenital tract—I shall describe one in association with ano-rectal gonorrhoea in the male—but primary involvement of the skin has been described (Thomson; Pugh; Lowry and Franks).

Many workers, I know, consider it to be impossible for the gonococcus to invade healthy stratified squamous epithelium of the epidermis, and it will perhaps be helpful if I mention here a few pathological facts. Bumm originally stated in 1885 that gonococci were never seen in the intercellular spaces of the stratified squamous epithelium of the cornea. Councilman in 1893, and after him Finger, Ghon and Schlagenhaufer, and many subsequent workers, showed that the gonococcus never penetrated the stratified squamous epithelium of the fossa navicularis urethrae. The only dissentients are Touton, Jadassohn, and Dinkler, but they all admit that penetration of this type of epithelium is rare. Dinkler found gonococci in the stratified squamous epithelium of the cornea, and both Touton and Jadassohn in the stratified squamous epithelium of excised para-urethral ducts, Touton stating that gonococci were seen in the intercellular spaces as far as the fourth layer of cells, but never deeper and never in the underlying

* An address to the Medical Society for the Study of Venereal Diseases, 20th May 1944.

subepithelial connective tissue, even though it was crammed full of round cells. Bockhart in 1883 failed to find any gonococci in the stratified squamous epithelium of the fossa navicularis, but the lymphatics in this region contained large numbers of them, which no doubt found their way there after penetrating the adjacent columnar epithelium. I have on two occasions excised para-urethral ducts infected with gonococci and not communicating with the urethra, but the pathologist was unable to demonstrate gonococci in sections, even though large numbers were found in the discharge before the excision was carried out. For some years now I have been investigating, in association with E. T. C. Milligan, the pathology of ano-rectal gonorrhoea ; we have never seen gonococci in the stratified squamous epithelium of the anal canal, in spite of the fact that they have been present in the subjacent subepithelial connective tissue.

I do not consider it to be possible for the gonococcus to penetrate a healthy epidermis, and in my opinion it is always necessary for the superficial layers to be destroyed before the organisms are able to gain a footing ; this may be the case also in primary infections of hair follicles. Persistent gonococcal discharges in the region of abrasions are, in my opinion, always present before infection of the epidermis can occur. In all my cases with genital lesions containing gonococci these were situated in the region of the median raphe, and I wondered whether or not this structure did at times contain a modified epithelium. With this possibility in view I examined many sections, but failed to verify this presumption. However, it can be definitely stated that penetration of the epidermis is not always necessary, as I have seen genital ulceration follow the rupture of multiple small abscesses along the course of a gonococcal lymphangitis or an infected para-urethral duct, and this may indeed be the pathology of all genital gonococcal ulcers. In this connexion it is noteworthy that Scholtz, as early as 1899, reported a subcutaneous gonococcal abscess on the dorsum of the penis, which developed in a nodular swelling on the course of an acute lymphangitis.

Small bullae, often single but sometimes multiple and usually in association with a long prepuce and profuse urethral discharge, are seen occasionally on the glans penis. They form, when ruptured, small superficial gonococcal ulcers, which are usually mistaken for herpes genitalis.

Diagnosis

Gonococcal ulcers situated on the skin are very similar to chancroids. They may be single or multiple, with undermining of the edges, but are painless and without induration. They will be found to harbour gonococci, and it is an easy matter to find the organisms in smears taken after thoroughly cleansing and then squeezing the lesions. Even when gonococci have been found, it is always advisable to carry out repeated examinations for *Spirochaeta pallida*, also blood examinations, as there is the ever-present possibility of a double infection. I have on two occasions seen both linear abscesses and ulcers (all harbouring gonococci) on the under surface of the penis ; one was considered to be due to a suppurative lymphangitis ; biopsy of the other showed it to be due to localized areas of suppuration along the course of an infected para-urethral duct.

It is also worth emphasizing that gonococcal infection of the two para-urethral glands (situated in the lips of the external urinary meatus), also of para-urethral channels, may be resistant to treatment, and that their openings on the surface may be mistaken for gonococcal ulcers.

Staining of gonococci in sections.—The following method, adapted by Dossett from that of von Wahl, who used it for staining smears, has been found to be very successful in demonstrating gonococci in sections.

(1) Bring section down to water.
(2) Stain for 30 minutes at 37° C. in the following mixture :

concentrated alcoholic auramine solution	2 parts
95 per cent alcohol	1·5 ,,
concentrated alcoholic thionine solution	2 ,,
concentrated aqueous methyl green solution	3 ,,
distilled water	6 ,,

(This stain was found to work better after being kept for at least a month.)

(3) Rinse in tap water.
(4) Dehydrate in 70 per cent, 90 per cent and 96 per cent alcohols, allowing 10 seconds in each.
(5) Complete the dehydration in absolute alcohol. (The alcohols also differentiate the section, final differentiation being controlled in the absolute alcohol. The time taken is usually from 30 seconds to 1 minute, when the section should have a pale blue appearance.)
(6) Transfer to chloroform for 1-2 minutes.
(7) Clear in xylene.
(8) Mount in a neutral mounting medium. (In ordinary balsam the sections fade.)

Staining reactions are as under.

Epithelial tissues—violet.
Connective tissue—cells, violet-blue, background, pale violet to colourless.
Gonococci—blue-black with a greenish halo.

Treatment

In the pre-sulphonamide era gonococcal ulcers on the skin were very resistant to treatment, but the superficial ulceration on the glans penis healed quickly when the discharge was brought under control. Only one case reported in the literature, that of Lowry and Franks, was resistant to the sulphonamides, and the electric cautery was necessary to effect a cure. No doubt penicillin is now the substance of choice in the treatment of these cases.

Cases with local lesions reported in the literature

Extra-genital lesions

Note should be made of the case described by Wright as occurring in hair follicles of a case of sycosis barbae, at a time when both the patient and his barber were suffering from acute gonorrhoea. Meyer also describes the case of a woman with acute gonorrhoea, in whom bullae developed on a finger ; in these gonococci were found in both smears and cultures. Pugh describes the case of an abscess in the skin overlying the sternum from which he obtained a pure culture of gonococci ; it occurred after sexual intercourse between the breasts. He also gives details of a primary gonococcal abscess in the axilla (after sexual intercourse), which may have been metastatic as it was complicated by an acute arthritis of the left ankle. Templeton records the case of a young Greek with a gonococcal infection of the umbilicus which was diagnosed shortly after the onset of a urethritis ; it was probably a direct infection of an intertriginous dermatitis of the umbilicus.

Genital lesions

Thomson records a case with gonococcal pustules on the ventral surface of the penis in the region of the median raphe ; the urethra was not infected. He also reports a primary gonococcal infection in a scabetic lesion on the ventral surface of the penis ; a pure culture of gonococci was grown from the lesion.

Lowry and Franks describe a case of primary gonococcal ulceration on the ventral surface of the penis ; there was no previous history of urethritis and no other foci of infection were detected. The infected ulcers were resistant to chemotherapy and their destruction by electro-coagulation was necessary to effect a cure.

Typical cases of genital lesions

The following cases came under my own observation.

The first case was in a man aged 28 years who had been treated for 6 months with medicine only for an attack of gonorrhoea. He was referred to me in August 1934 with a sore on the prepuce of one month's duration. On examination there was found to be a profuse urethral discharge containing gonococci, and the urine was muddy in all glasses. There was a non-indurated painless ulcer, with undermined edges and a sloughy base, on the skin of the prepuce in the region of the median raphe, and, when the prepuce was in its normal position covering the glans, it was noted that the ulcer was in direct apposition to the external urinary meatus. There was no adenitis and scrapings from the ulcer were repeatedly negative for *S. pallida* and Ducrey's bacillus ; the Wassermann and Kahn reactions were also negative. The urethral infection reacted rapidly to urethro-vesical irrigations twice daily with

potassium permanganate, as it always does when local treatment has been delayed for long periods, but the ulcer instead of healing increased slightly in size. Smears from the ulcer showed large numbers of gonococci, both intracellular and extracellular in position, and a pure growth was obtained in culture. The ulcer proved to be very resistant to treatment, which consisted of frequent bathing in warm solutions of potassium permanganate, 1 in 2,000, and the application twice daily of silver nitrate, 2 grains to the ounce. Smears from the ulcer remained positive for 2 months and the ulcer did not heal until a fortnight later. The ideal treatment would have been circumcision, but the patient refused operation. He did, however, insist on circumcision before marriage 2 years later.

My second case, a labourer aged 24 years, was admitted to hospital under my care in November 1934 with multiple superficial linear abscesses and one ulcer of 2 weeks' duration on the under surface of the penis in the region of the median raphe. The previous history showed that he had been under treatment for gonococcal urethritis for 2 months. On examination there was a gonococcal urethral discharge, and smears from the ulcer and pus aspirated from an abscess contained gonococci; cultures were also positive. The ulcer was excised and gonococci were also found in the sub-epithelial connective tissue; no organisms were seen in the epidermis. Repeated scrapings were negative for *S. pallida* and Ducrey's bacillus; the Wassermann and Kahn tests carried out at weekly intervals were negative and the gonococcal complement fixation test was weakly positive on one occasion only. All the abscesses eventually broke down to form ulcers, which were resistant to treatment. The patient insisted on his discharge from hospital (about 5 weeks after admission) with two unhealed ulcers which did not contain gonococci.

My third case occurred in a man aged 27 years suffering from primary ano-rectal gonorrhoea. A small superficial ulcer, not indurated and with undermined edges, was situated in the median raphe just anterior to the anus; no tract communicating with the anal canal could be detected. There was no urogenital infection, but ano-rectal smears showed large numbers of intracellular and extracellular gonococci; Wassermann, Kahn and gonococcal complement fixation tests were negative and remained so throughout the period of observation. Smears from the ulcer were positive for gonococci and negative for *S. pallida*; there was no enlargement of the lymphatic glands. The ulcer, as in the two previous cases, was resistant to local treatment and did not heal until 6 weeks had elapsed.

Systemic metastatic lesions

Systemic skin lesions, which usually occur during the course of a gonococcal septicaemia, may consist of simple erythema, erythema multiforme, erythema nodosum, purpura, vesiculo-pustular eruptions and subcutaneous abscesses. Krepschmer (cited by Hauck) considers that these metastatic eruptions occur only when there are complications such as arthritis or conjunctivitis, and that the rashes are due to emboli of gonococci arising from such complications.

Simple erythema, erythema multiforme, erythema nodosum and purpura

These lesions are said to occur during the acute stage of the disease. I have never been convinced that they are gonococcal in origin and have considered them in many cases to be rashes due to drugs. Biopsies have been carried out on some of my cases, but the pathologist has always failed to demonstrate gonococci. Redewill states that Ichikama and Olimori in 1933 demonstrated gonococci in erythematous lesions. Dorner cultured the gonococcus in small pustules which developed in a morbilliform roseolar eruption. Hodara obtained positive blood cultures from a soldier in whom purulent and haemorrhagic bullae had developed in a generalized erythematous eruption, but he does not mention whether or not gonococci were found in the skin lesions. Paschen and Jentz reported a case with a generalized and slightly raised petechial eruption in which gonococci were demonstrated in sections.

In the pre-chemotherapy era I often saw, during a course of copaiba or sandalwood oil, irritating macular and papular eruptions, occasionally generalized but more often localized on the lower limbs, which, when the drug was omitted, quickly disappeared. In a case of acute uncomplicated gonorrhoea recently under my care, a purpuric eruption developed on the right forearm on the fourth day during a course of sulphathiazole given in doses of 1 gramme every 6 hours. This, in my opinion, was due to the drug.

Sutton and Sutton quote van Krieken's case of annular erythema in a girl aged 7 years who was suffering from gonococcal vulvovaginitis. Hauck in 1935 was able to find only 30 cases of purpura associated with gonorrhoea recorded in the literature. Bakst, Foley and Lamb reported the development of lesions of

erythema nodosum in a case of gonococcal septicaemia, and on 2 occasions I have seen similar lesions in patients who were suffering from gonococcal arthritis. Biopsy in one of my cases did not reveal the presence of gonococci in the lesions ; this was also the case in the biopsy carried out by Bakst, Foley and Lamb. Erythema nodosum may occur also during intensive therapy with sulphathiazole, but in my experience it does not occur during short courses when moderate doses are used.

Vesiculopustular eruptions

These occasionally occur during the course of a gonococcal septicaemia. In one case, similar to that described by Lidström (wrongly, I think) as a case of keratodermia blennorrhagica, I found gonococci in small vesiculopustular lesions on the abdomen in a case of gonococcal septicaemia. The lesions were superficial and did not subsequently develop into parakeratotic patches or nodules. Lidström's case showed "small blisters", varying in size from a pin's head to a hempseed, situated chiefly on the thighs, in a fatal case of gonococcal septicaemia with polyarthritis and endocarditis. The contents of the vesicles showed gonococci in both smears and cultures, but it is interesting to note that gonococci were not detected in urethral smears, neither were they found in the synovial fluid of an acutely inflamed knee which was aspirated early.

Hauck quotes Liebe, as finding gonococci in a bullous eruption on the palms and cheeks of a child 4 days old, and Henning, as having cultured gonococci from similar lesions in a child 4 years old. Siegel in 1925 described a case (similar to those previously recorded by Bloch and Hébert, and by Achard and Mouzon) of gonococcal septicaemia with a generalized haemorrhagic papular eruption. Some of the lesions developed into haemorrhagic vesicles and pustules containing pus cells and gonoccoci.

Subcutaneous abscesses

The occurrence of these during the course of a gonococcal septicaemia, associated with cutaneous lesions of the erythema nodosum type, was described by Scholtz in 1899. Red and painful lesions of erythema nodosum, which became necrotic in the centre, developed on the trunk, left leg and left elbow. At this stage no organisms were found in the lesions, but when they broke down to form subcutaneous abscesses large numbers of gonococci were found in the pus ; cultures were also positive. Barrett describes a case with a solitary gonococcal subcutaneous abscess on the scalp, which is unique, as it was in association with typical lesions of keratodermia blennorrhagica. However, in all the multiple metastatic subcutaneous abscesses that I have seen, the organism responsible has been *Staphylococcus aureus*. The patient, in one particular case, was admitted under my care in 1934 with a prostatic abscess, and smears of the urethral discharge contained gonococci. The abscess ruptured into the rectum, and a few days later staphylococcal pyaemia with a right perinephric abscess and multiple subcutaneous abscesses developed ; necropsy showed also the presence of a carbuncle of the kidney.

Keratodermia blennorrhagica

The most distinctive skin eruption seen in association with gonorrhoea is keratodermia blennorrhagica. It was first described by Vidal in 1893 and two years later a case was recorded by Jeanselme. Vidal gave a complete clinical description and stated that anti-syphilitic treatment had no effect on the lesions. The first case reported in England was by Sequeira in 1910 (a further case being reported by Williams a few months later and one in America by Simpson in 1912). Under 100 cases have so far been reported in the literature ; indeed Harrison stated in 1931 that the incidence was 1 in 5,000 cases of gonorrhoea ; Brown and Hargreaves in 1917 gave it as 1 in 6,666. It usually occurs in males and only 9 cases have been recorded in females (Robert (who also reports Dumany's case) in a child aged 4 years ; Buschke ; Isaac ; Sutter ; Lees ; Buschke and Langer ; Wayson ; C. A. Falk).

I have been fortunate in collecting from various venereal disease clinics 20 cases, many of which were admitted under my care at St. Charles' Hospital. The records of these cases are given below. The patients were sent into hospital with a diagnosis of gonococcal arthritis, but the skin lesions were rarely diagnosed before admission. The lesions are usually symptomless, and unless a special examination is made in all cases of arthritis, the diagnosis will often be overlooked. This examination was always carried out soon after admission in cases of arthritis; my orderlies, who were trained to be on the look-out for it, often diagnosed the condition before I had seen the case myself.

The syndrome

A clinical syndrome is associated with the eruption and consists of (1) urethritis, (2) polyarthritis, with or without other metastatic complications, (3) cachexia and (4) pyrexia.

Urethritis.—The urethritis may be gonococcal or non-gonococcal. We failed to find gonococci in 10 cases, but in 3 of these they had been found before admission (once in the synovial fluid aspirated from a joint) and in one the evidence was inconclusive. There were therefore 6 cases in which gonococci were not found in the urethral secretions, but one of these gave a doubtful and another a strongly positive gonococcal complement fixation test result, which, as is often the case, may have been due to previous attacks of gonorrhoea. In 18 of my cases there was a previous history of one or more attacks of gonorrhoea (often severe and complicated with polyarthritis and other metastatic or local lesions) but never of skin eruptions.

I have found 16 cases of keratodermia blennorrhagica described in the literature in association with the syndrome of Reiter's disease and therefore considered to have no connexion with gonorrhoea. In 7 of these cases (Wiedmann; Kuske, 2 cases; Löhe and Rosenfeld; Buschke; Launois; Baerman) there was a previous history of gonorrhoea; in Launois's case there had been 5 previous attacks.

The remaining cases are those of Naegeli[1], 2 cases; Kuske, 2 further cases; Löhe and Rosenfeld, 1 further case; Lojander; Kruspe; Lever and Crawford. Naegeli does not mention the previous history in his first case, in which the lesions were rupia-like; in his second case the eruption (which he describes as psoriasiform) was provoked by treatment with radiant heat and 10 per cent ichthyol in vaseline. In Kuske's first case there was a previous history of syphilis and the lesions resembled rupia; in his second case (which was also provoked) the lesions on the soles of the feet were soft and not keratotic. In my opinion the two cases of Lever and Crawford, case 2 in both the Naegeli and the Kuske series, and the cases of Lojander and of Löhe and Rosenfeld, were examples of psoriasis rupioides and not of keratodermia blennorrhagica; indeed Löhe and Rosenfeld admit that the skin lesions in their case subsequently developed into a typical psoriasis vulgaris. It is interesting to note that in Lojander's case there was no urethritis or urinary infection; here again the lesions were provoked by macerating the skin with wet dressings. Lever and Crawford quote Kruspe, but I have been unable to obtain a copy of his paper. Some of the cases described in the literature as having no connexion with gonorrhoea are certainly typical cases of keratodermia blennorrhagica; on the other hand many of them are not so. In my own series, as already mentioned, there are 4 (possibly 6) such cases.

Arthritis.—All my cases of keratodermia blennorrhagica and all but 4 of those recorded in the literature (Robert, who also cites Dumany's case; Roth; C. A. Falk) were associated with arthritis.

Dumany's case was complicated with iritis and conjunctivitis. The one described by Roth was associated with teno-synovitis of the extensor tendon of the right great toe, and in my opinion there was also involvement of the right mid-tarsal joint. Falk's patient had both gonorrhoea and syphilis (Wassermann positive) and the lesions on the dorsum of the hand were admitted by him to resemble rupia very closely. Treatment for syphilis no doubt aided resolution considerably, for the patient was discharged cured after less than a month's treatment.

The arthritis, which involved more than one joint in all my cases, was usually acute.

Cachexia and pyrexia.—Fourteen patients were really ill and cachectic. There was a swinging temperature with other signs of systemic infection in 16 cases: 2 cases were apyrexial.

Other metastatic complications.—As already mentioned, all of my cases suffered from polyarthritis. Further joints became involved in 8 during treatment, in 3 of which at the same time a fresh crop of vesicles developed. In 5 there were no other metastatic complications. There were 10 cases with conjunctivitis (9 bilateral and 1 unilateral), 3 with iritis (1 bilateral and 2 unilateral), one with endocarditis and pericarditis, 2 with tachycardia, 2 with bursitis and one with teno-synovitis.

Description of eruption

In my opinion there are clinically two types of lesions: (1) the hard parakeratotic nodules (see Plates A and B, C, and E) and (2) the soft limpet-like parakeratotic patches (see Plates D, F, and G); both types may be present in the same patient.

Parakeratotic nodules.—The first type passes through 3 distinct stages: vesicular, pustular and keratotoic. The primary lesions are discrete vesicles which quickly increase in size. It has been said that the vesicles occasionally coalesce to form bullae. In one of my cases (Case 3) there was a large bulla in association with multiple vesicles on the sole of the left foot; it was a discrete lesion in the first place but the increase in size was not due to the coalescing of vesicles. Within 24 hours all the vesicles show a yellow tint (becoming pustules) and at the same time a distinctly palpable thickening is seen and felt in the centre of the roof of all pustules. This thickening soon extends both to the periphery and to the contents of the pustules and results in the typical parakeratotic nodules from which the disease derives its name. Spontaneous rupture of vesicles or pustules has not been observed. In all 3 stages there are no local signs or symptoms of an acute inflammatory reaction. The vesicles occur in crops and, at the same time in one area, I have seen vesicles, pustules and parakeratotic nodules. In my cases there was usually a high temperature with an acute exacerbation of the arthritis, occasionally with involvement of further joints, when the crops of vesicles appeared. No increase in the urethral discharge (such as has been reported in the literature) was noted, but in a few cases other metastatic complications developed. The parakeratotic nodules, light brown in colour, are of brick-like consistency, are situated on the surface of the skin, and vary in size from that of hempseed to a two-shilling piece; the epidermis surrounding the nodules is, in my experience, rarely thickened. French writers liken the lesions to mountain ranges on a relief map. The contents of the vesicles and pustules are referred to below in the discussion of aetiology.

Soft lesions.—The soft parakeratotic lesions consist of many layers of scales, which are often heaped up centrally and resemble rupia; they are all discrete and in my experience do not contain parakeratotic nodules. Removal of scales, when the lesion is recent, leaves a weeping surface (due to exposure of the corium) and the scales soon reappear but to a lesser extent. In the older lesions the exposed surface is invariably dry.

In all my cases the lesions of keratodermia blennorrhagica on the soles of the feet were discrete and of brick-like consistency. The parakeratotic nodules were not covered with heaped-up scales and bore no resemblance to the parakeratotic limpet-like lesions which appear usually on the seborrhoeic areas (scalp, chest and back) and on the mucous membrane of glans and prepuce. This finding is not in agreement with many of the cases described in the literature. It may be explained by the fact that the deposit of several layers of scales on the lesions situated on the soles of the feet may have been due to the effects of local treatment which rendered the area sodden. In my cases no treatment had been prescribed. There may, however, be an anatomical explanation. The epidermis of the soles of the feet is much thicker (1·4 millimetres) than it is in other parts of the body, and this is not only the result of external mechanical causes, as it is also well developed in the foetus; it contains sweat glands but not sebaceous glands,

and the absence of the latter may be the determining factor. In my series the limpet-like lesions were usually seen in the seborrhoeic areas. These parts are rich in sebaceous glands and their semi-fluid secretion of fat and broken-down epithelial cells favours the formation of this type of lesion. It is admitted that typical parakeratotic nodules on the glans penis, which does contain sebaceous glands but no sweat glands, were seen in 5 of my patients, but 4 of them had been circumcised ; the surface of the glans was dry and no doubt many of the sebaceous glands had atrophied ; the surface of the glans was also dry in the remaining case because the prepuce was retracted. When the prepuce covered the glans the lesion was always a parakeratotic balanitis, consisting of heaped-up layers of scales which did not contain hard parakeratotic nodules.

Distribution of eruption

Parakeratotic nodules.—The nodules show a predilection for the soles of the feet, where they are usually symmetrical. In 14 of my cases they occurred on the soles of both feet and in 3 further cases (one of which was provoked by radiant heat and the application of ichthyol) on the sole of one foot only.

The glans penis was involved in 5 cases, once alone and 4 times in association with lesions elsewhere. Lesions on the glans penis often precede those in other parts of the body. In 2 cases only were the parakeratotic nodules generalized. (See Case 10.) No nodules occurred on the upper limbs.

Soft parakeratotic patches.—They occurred on the scalp in 3 cases, and in one of these a similar lesion developed on the back during a course of sulphanilamide. A further case showed a hyperkeratotic area surrounding the right nipple, but this may have been due to scabies. Here again, in my series, no lesions occurred on the upper limbs. Parakeratotic balanitis, usually referred to as balanitis circinata, was noted in 9 cases, all of which were in association with lesions, usually nodular, in other parts of the body. In 2 of these the mucous membrane of the prepuce only was involved and in 2 there were at the same time parakeratotic nodules on the glans penis. I have on several occasions seen balanitis circinata in association with polyarthritis and other metastatic complications, and even though this condition often precedes nodular or parakeratotic patches in other parts of the body, I have not included such cases in this series.

The soft limpet-like lesions, unaccompanied by hard parakeratotic nodules, occurred in only one of my cases. (See Case 7.)

Oral lesions.—These consist of flat papules or vesicles on the buccal mucous membrane and hard palate and have been reported by Stanislawski, by Chambers and Koetter, by Sherman, Blumenthal and Heidenreich, and by others. In Chambers and Koetter's case 4 crops of slightly elevated flat papules, histologically identical with the skin lesions, occurred on the hard palate, tongue and buccal mucous membrane. Septic mouths were noted in several of my cases, but in only one were vesicles and superficial ulcers noted on the buccal mucous membrane and hard palate ; the lesions coincided with a crop of vesicles on the soles of both feet. No doubt many oral lesions were overlooked.

Corneal lesions.—Epstein and Chambers describe corneal lesions in 2 cases ; papules or vesicles, developing into erosions within 48 hours, appeared at the same time as did crops of typical lesions in other parts of the body.

Histology

Histologically there is a similarity between the lesions of keratodermia blennorrhagica and psoriasis ; perhaps it will be helpful first to consider the latter.

In psoriasis vulgaris the main changes are found in the epidermis, which exhibits the following conditions.

(1) Acanthosis, which affects the interpapillary part, mainly resulting in a lengthening and broadening of the interpapillary processes. The suprapapillary zone is however thinned and frequently consists of 1-3 layers of cells.

(2) Absence of stratum granulosum.
(3) Parakeratosis.
(4) Intercellular oedema with immigration of leucocytes from the corium, where they are usually found sparsely scattered. These leucocytes sometimes collect into small foci beneath the stratum corneum, giving rise to the pseudo-abscesses of Munro (Macleod and Muende).

In pustular psoriasis, the pathological findings are similar, except that the pseudo-abscesses of Munro are usually much larger, and the parakeratosis not so well marked, there being a considerable amount of keratosis too. In psoriasis rupioides the scales are heaped up centrally into rupia-like crusts which lose their silvery appearance.

In keratodermia blennorrhagica the acanthosis, although affecting the interpapillary zone chiefly, also affects the suprapapillary zone, and the intercellular oedema is usually much more marked in the upper part of the epidermis, giving rise to a honeycombing (spongiosis) in the meshes of which there are numerous freely-lying leucocytes. The horny layer is much thickened, and although the cells are chiefly nucleated, the layers do not flake off as freely as they do in psoriasis and there is a tendency towards keratinization. The pars papillaris is oedematous, the capillaries are congested, and the tissue contains a large number of lymphocytes and few polymorphonuclear leucocytes.

Biopsies, in my cases, were carried out only on the first type of lesion (vesicle, pustule and nodule) but both types are the same histologically. Chambers and Koetter found similar changes in oral lesions.

Differential diagnosis

From acrodermatitis perstans.—There is a variety of pustular erythematous and scaly or crusted eruptions on the feet and hands, appearing as single plaques (for example, on the ball of the thumb or on the instep), or as multiple lesions on the extremities, which are variously described as acrodermatitis perstans, pustular bacteride or in some cases pustular psoriasis. The eruption is represented by red areas with a scaly undermined margin ; numerous pin-head pustules, at first sterile, are scattered over the surface. The condition is more often mistaken for ringworm than for keratodermia, which differs in the heaped-up horny character of the individual discrete lesions.

From psoriasis rupioides.—Psoriasis rupioides, in which the scales are heaped-up centrally into horny-looking cones and associated with rheumatoid arthritis, often bears a close resemblance, both clinically and histologically, to keratodermia blennorrhagica. In these cases skiagrams of the joints show bony changes, whereas in keratodermia these would seem to be extremely rare and were noted in only one of my cases. (See Case 2.) In Adamson's cases of arthropathic psoriasis some of the skin lesions were indistinguishable from those of keratodermia blennorrhagica, but in many of his cases there were also typical lesions of psoriasis vulgaris in other parts of the body. In cases of pustular psoriasis I have myself seen the hyperkeratotic areas on the soles of the feet, which were soft and easily differentiated from the keratotic nodules of keratodermia blennorrhagica. Psoriasis is a recurring disease and is rarely associated with severe toxic symptoms.

The lesions on the soles of the feet in many cases of keratodermia blennorrhagica described in the literature consist of heaped-up patches of scales and not of parakeratotic nodules and, in my opinion, these are indistinguishable from the lesions of psoriasis rupioides ; in my cases, the lesions on the soles of the feet were always hard parakeratotic nodules.

The gonococcal complement fixation reaction of the blood serum may sometimes be helpful in the differential diagnosis, but it must be remembered that there is a previous history of gonorrhoea in many cases of keratodermia blennorrhagica (this was so in 18 of my cases) and gonococcal antibodies, when once formed, may persist throughout life. There may also be false positives—and positives evoked by the administration of gonococcal vaccines. In my series this test was carried out (usually at weekly intervals) on 18 cases. On admission 6 were positive, 9 negative (4 in spite of the fact that gonococci were present in the urethral discharge) and 3 doubtful. Of the negative reactions 8 remained negative throughout the period of observation and one became positive 6 weeks later ;

the 3 doubtfuls subsequently became positive and were possibly evoked by intramuscular injections of gonococcal vaccine.

The limpet-like discrete parakeratotic patches seen in my cases may be mistaken for syphilitic rupia, but in the latter the lesions are usually unilateral ; there may be other signs of syphilis and the serum reactions will be positive.

Aetiology and bacteriology

Gram negative diplococci, morphologically indistinguishable from gonococci, have been found in smears from the lesions (Wadsack ; Gager ; Campbell ; Thomson ; Du Bois ; Lidström ; Barrett).

Du Bois and Lidström also identified the organisms in culture. Lidström's case was, as already mentioned, a typical case of metastatic vesiculopustular eruption and not keratodermia blennorrhagica ; in Du Bois's case, too, the skin lesions were more like those of a generalized metastatic pustular eruption. Pustules containing large numbers of pus cells developed in macules situated only on the front of the chest and abdomen, and it was not until 5 weeks later that impetiginous lesions, which bore no resemblance to keratodermia blennorrhagica, developed on the hands and feet. Besides extracellular diplococci, Gager found also large numbers of pus cells in the pustules ; this too was in all probability a metastatic pustular eruption. In Barrett's case Gram negative intracellular diplococci were found in smears made from macerated crusts, but the eruption was associated with a metastatic subcutaneous abscess on the scalp which contained gonococci, and the scales examined may have consisted of inspissated pus from another subcutaneous abscess which had ruptured spontaneously.

Wadsack's case was, in my opinion, a generalized squamous papular eruption, associated with polyarthritis and pericarditis, and not keratodermia blennorrhagica. He claims to have found one pair of Gram negative diplococci, intracellular in position, in the serum expressed from a papule, and also to have demonstrated them in sections of a papule. In the discussion which followed the reading of Wadsack's paper, Reckzeh suggested that the so-called gonococci were a precipitate from the stain. I have been unable to find details of the cases of Thomson and of Campbell.

The development of vesicular and pustular lesions on the soles of the feet was observed in 8 of my cases and in 4 there was more than one crop. Smears, cultural examinations and biopsies were carried out in each case and on no occasion were gonococci seen or grown. Aspiration from the vesicles showed epithelial cells but no pus cells or organisms ; cultures were always sterile. The contents of the pustules, too, consisted chiefly of epithelial cells, many of which were degenerated, with very few pus cells ; cultures were sterile. Occasionally in a small number of culture tubes there was a small growth of *Staphyloccus albus* or of diphtheroids, which was considered to be a contamination. Dr. Goodhart, who carried out much of the laboratory work, expressed to me the view that, from the nature of the cell exudate and the absence of pus, it was extremely unlikely that gonococci would be found.

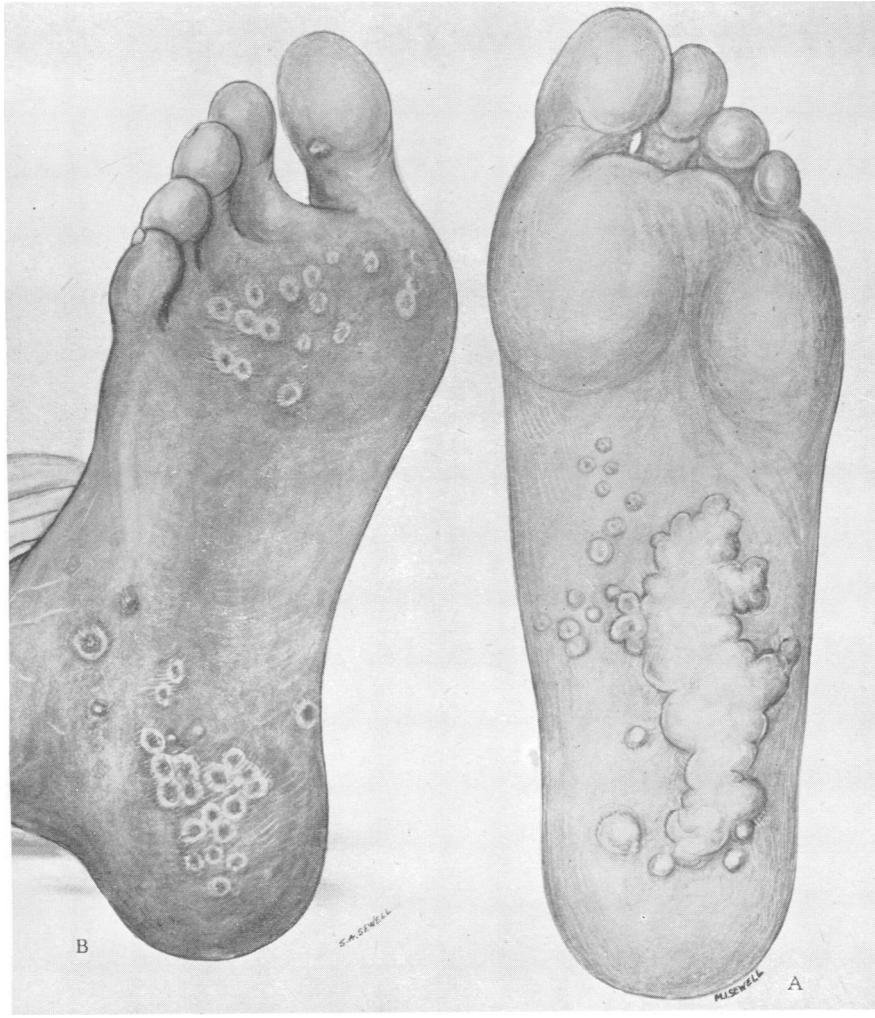
The disease often runs a septicaemic course and it is surprising that blood cultures reported in the literature, have been with one exception (Sutter) negative. They were carried out in 9 of my cases.

Sutter's case occurred in a little girl aged 2½ years who had vulvovaginitis, which was complicated by a gonococcal septicaemia with polyarthritis, peritonitis, otitis media, stomatitis and skin eruptions. Gonococci were found in pure culture in the discharge from the vagina, ear, mouth and abdominal fistula. A macular eruption was noted early in the disease ; 6 months later the reappearance of gonococci in the vaginal secretions was associated with a scarlatiniform rash. Subsequently there was a generalized vesicular eruption, the vesicles varying in size from a pin's head to a five-shilling piece. All lesions became crusted and developed into typical soft parakeratotic patches ; there were no lesions on the palms or soles. Blood cultures were positive when the child's temperature registered 100·4° F. Roark has been wrongly reported in the literature as obtaining positive blood cultures in his case of keratodermia blennorrhagica ; one blood serum tube culture yielded a pure growth of a large Gram negative diplococcus, which was considered by him to be a contamination.

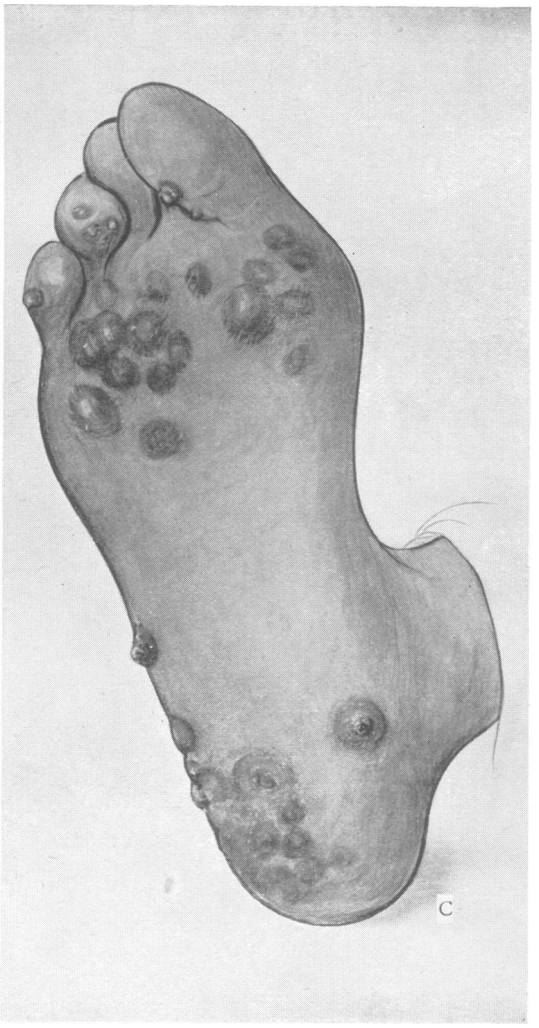
Jeanselme stated in 1895 that the disease was due to the circulating toxins of the gonococcus, which acted either directly on the skin or on the nerves, thereby producing trophic changes. Naegeli and Kuske both consider keratodermia blennorrhagica to be a manifestation of Reiter's disease and to have no connexion with gonorrhoea, whereas Löhe and Rosenfeld maintain that it is caused by a chemical irritant arising from the damaged cartilage of the affected joints.

Chauffard and Fiessinger in 1909 reproduced typical lesions by scarifying the skin and rubbing in the exudate from a macerated keratotic nodule ; Lees and Percival later

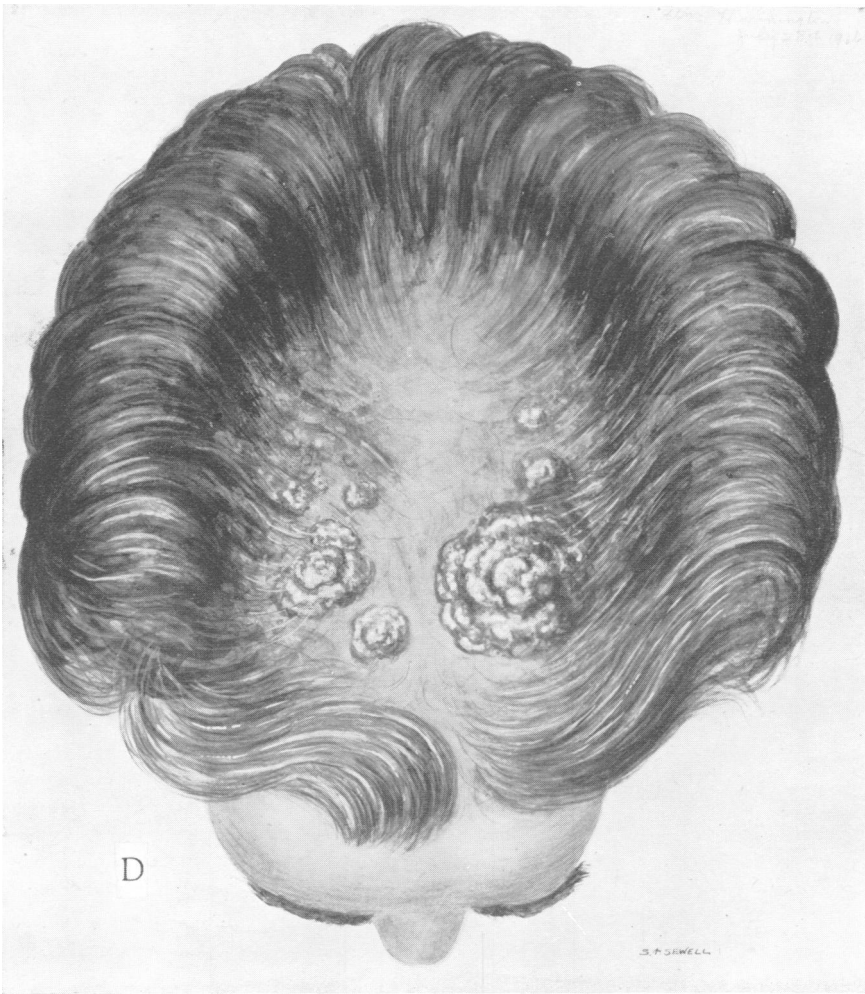
A, B, C and E are Type I and D, F and G Type II lesions of keratodermia blennorrhagica; B, C, D and G, showing Type I and Type II lesions, are from the same patient (Case 8).



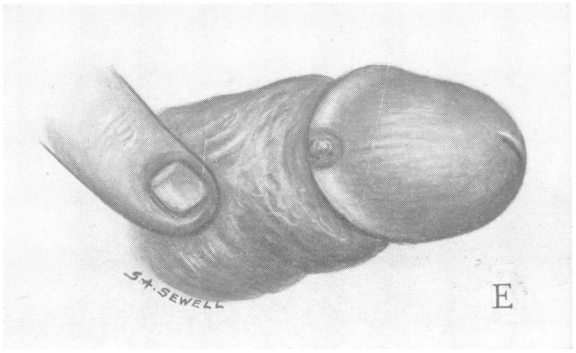
A and B show early vesicular and pustular lesions developing into hard parakeratotic nodules. (Thickening first seen and felt in centre of roof of pustule.)

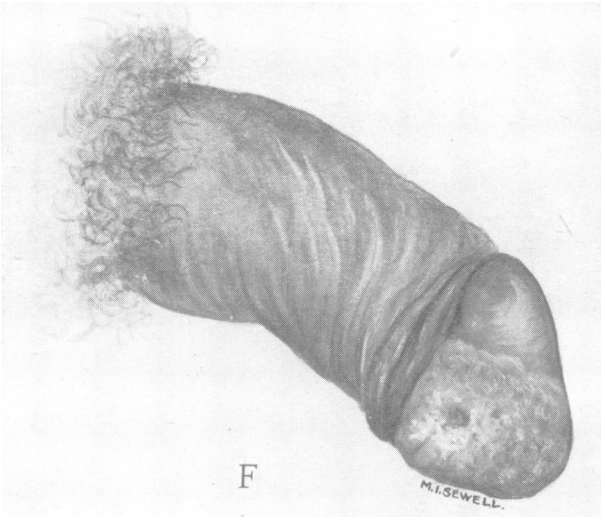


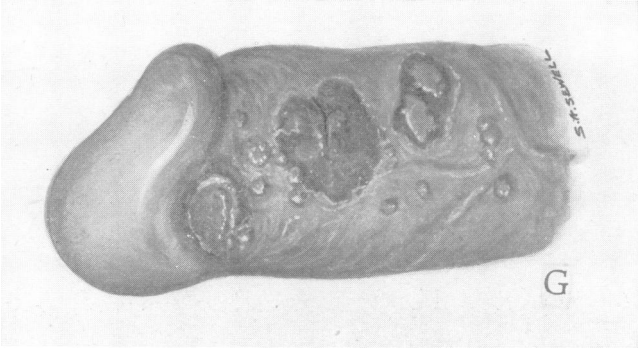
C.—Hard parakeratotic nodules.



D.—Soft limpet-like parakeratotic patches on scalp.







E.—A hard parakeratotic nodule on glans penis.

F.—Soft parakeratotic patch on glans penis.

G.—Localized areas of balanitis—24 hours after removal of soft parakeratotic patches.

reproduced a keratotic nodule by the intradermal injection of gonococci, *Staph. albus* and diphtheroids—the organisms cultured from the urethral discharge. This nodule, as they say, may have been due to the organisms, to a fresh lesion occurring spontaneously at the site of inoculation or to Koebner's phenomenon. Lesions have been provoked in patients with Reiter's disease by exposure to radiant heat and by the application of 10 per cent ichthyol in vaseline (Naegeli[2]; Kuske) and by macerating the skin with wet dressings (Lojander). In one of my cases (Case 18) lesions were provoked by treatment with radiant heat and 10 per cent ichthyol in vaseline.

The lesions under review may be due to gonococcal toxins but, judging from the work of others and the investigations of my own cases, I cannot believe that they are due to the gonococcus. The organism has been found once only in the blood stream, and I have already brought forward evidence to show that it is questionable whether it has ever been found in the lesions themselves. I consider that the lesions are probably due to a virus—a pure infection or a mixed one in association with gonorrhoea.

It is worth noting in this connexion that certain types of minute pleuropneumonia-like organisms cause polyarthritis in rats and mice. The organisms are virus-like and appear as rings, granules and comma-shaped structures, which, in one phase of their development, are filter passers and do not grow on ordinary media. One type (L4), described by Woglom and Warren as a pyogenic virus, invariably causes arthritis in rats and mice when injected in the pad. Furthermore, arthritis is seen in goats affected with contagious agalactia, the infective agent of which is also in the group of pleuropneumonia-like bodies, and there is also inflammation of joints in bovine pleuropneumonia (Findlay, Mackenzie, MacCallum and Klieneberger). The fact that a polyarthritis due to pleuropneumonia-like organisms occurs in certain animals may have some bearing on the aetiology of keratodermia blennorrhagica. In some of my cases of keratodermia blennorrhagica the elementary bodies have been accompanied by a small number of rings, suggesting that the rings are developing from the granules: it may be the granular stage in the development of pleuropneumonia-like organisms.

Mixed infections of gonococcal and non-gonococcal urethritis certainly seem to occur more frequently than is generally supposed, their diagnosis having been made possible since the introduction of the sulphonamides and of penicillin, and this, I maintain, is the main cause of the rise in the number of cases of non-gonococcal urethritis. Patients diagnosed as having gonorrhoea who react favourably to the sulphonamides or penicillin may have residual non-gonococcal infections; these, in the past, were considered by many authors to be due to deep-seated gonococci. In a recent case, smears of the residual urethral discharge (taken after treatment with 100,000 units of penicillin, given elsewhere) contained inclusion bodies. The fact that condylomata acuminata are seen in association with acute gonorrhoea and that Thygeson and Stone (also other authors) have demonstrated inclusion bodies in acute gonorrhoea, definitely confirms the occurrence of primary mixed infections.

Reiter's disease and keratodermia blennorrhagica

Reiter's disease is, in my opinion, a variety of non-gonococcal urethritis with metastatic complications, but the organisms cultured from the urethral discharge, which are often the normal bacterial flora of the fossa navicularis, may, it seems to me, have nothing to do with the infection. Gonococci are not, as some authorities suppose, lurking undetected in the background—I have never at a later date found gonococci in any cases which were originally diagnosed by me as suffering from primary non-specific urethritis—and the disease may even in some cases be due to a virus.

During the last 2 years I have had 5 cases of Reiter's disease with non-gonococcal urethritis, polyarthritis and conjunctivitis (2 without skin lesions) and in all of them inclusion bodies were found in the discharge from both the urethra and conjunctiva. I have on many occasions found inclusion bodies in the urethral discharge in cases of primary uncomplicated non-gonococcal urethritis, but so far in only one of my cases (Case 20) have metastases developed. In this connexion it is well worth noting a recent case of Reiter's disease (Case 18 in this series) in which inclusion bodies were found in the urethral discharge and the conjunctival secretion. Vesicles on the soles of the feet were provoked by the application

of 10 per cent ichthyol in vaseline, but unfortunately they had reached the nodular stage when first seen and an opportunity was lost to examine the clear vesicular secretion. Slides made from macerated nodules showed suspicious bodies in the cytoplasm of the epithelial cells, but the evidence was inconclusive.

Smears taken from 2 patients with early vesicular lesions, 9 and 10 years ago respectively, showed what appeared to be inclusion bodies in one of them, but owing to granular deposits elsewhere the results were not definite. However, through the courtesy of Lt.-col. King, I have recently had an opportunity of examining a case of Reiter's disease with typical parakeratotic nodules on the soles of both feet. I excised a nodule and took from the denuded area scrapings which, under microscopic examination, showed the presence of inclusion bodies. Synovial fluid aspirated from one of the infected knee joints has been injected into a volunteer's urethra. The inoculation was carried out 17 days ago and yesterday there was a slight urethral discharge, but as yet no inclusion bodies have been seen. Two further cases (Cases 19 and 20) were subsequently examined and in both of them inclusion bodies were found in the urethral discharge, conjunctival secretion and skin lesions. I have recently examined specimens from the skin lesions of a case of keratodermia blennorrhagica under the care of Dr. J. R. Crumbie; again (this is the fourth time) I observed large numbers of inclusion bodies. Thus in each case of keratodermia blennorrhagica that I have examined for inclusions they have been shown to be present.

It appears that Naegeli[1] and Kuske are right in considering that keratodermia blennorrhagica is a manifestation of Reiter's disease. Other workers in this field may confirm my opinion that the disease is due to a virus.

Clinical comparison of psoriasis with keratodermia blennorrhagica

We have already seen the close similarity between the histopathology of psoriasis and of keratodermia blennorrhagica. Clinically, too, the rupioid eruptions seen in arthropathic psoriasis are often indistinguishable from the soft parakeratotic patches in keratodermia blennorrhagica. The pathogenic agent may be the same in both diseases; indeed Lipschutz described eosinophilic inclusion bodies in the prickle-cell layer of the epidermis in early lesions of psoriasis (Macleod and Muende). Attempts to reproduce the disease by inoculation were successfully carried out by Destot (Hallopeau); other investigators have so far failed to do this.

Treatment of keratodermia blennorrhagica

Various treatments, some ingenious and all (in my opinion) unnecessary, have been recommended for the skin lesions. I have never prescribed treatment in cases of mine, except once when a parakeratotic nodule developed under the nail of the right great toe, causing a good deal of pain, and had to be excised.

Treatment should be concentrated on the primary focus of infection, the blood infection, the polyarthritis and other metastatic complications which may be associated with the condition. Chemotherapy, in the cases harbouring gonococci and not showing drug resistance, will deal effectively with the gonococcal urethritis and will clear up the blood infection; it may also eliminate susceptible types of non-specific organisms if they are present in the secretions. Urethrovesical irrigations are also helpful in dealing with virus infections and infections due to non-specific organisms. Penicillin may be superior to the sulphonamides and should be prescribed in all cases of drug resistance; in the few cases which I have so far observed it has had no beneficial effects on non-gonococcal urethritis due to virus disease.

Fever therapy is, in my opinion, the treatment of choice in the sulphonamide and penicillin failures. In the past, as will be seen in the description of my cases below, mild protein shock in the form of a mixed gonococcal vaccine (gonococci, 500 million, staphylococci, 1,000 million, diphtheroid bacillus, 200 million, streptococci, 100 million, and coliform bacilli, 100 million, per cubic centimetre) was given intramuscularly at 5-day intervals; beneficial effects followed its use. When this treatment failed, high fever was induced by the intravenous injection of Dmelcos vaccine or of triple typhoid vaccine (anti-typhoid-paratyphoid, T.A.B.).

In practice, fever therapy will be found to be the most effective form of treatment. Organic gold preparations are highly active in preventing arthritis due to pleuropneumonia-like organisms in rats and mice (Findlay, Mackenzie,

McCallum and Klieneberger); they may be helpful in the treatment of keratodermia. Case No. 20 is receiving this form of treatment.

Case records of keratodermia blennorrhagica.

Case 1

W. L., a labourer aged 31 years, was admitted (15.7.29) with non-specific urethral discharge, polyarthritis, bilateral conjunctivitis and keratodermia blennorrhagica. There was a previous history of gonorrhoea in 1925. He had attended a hospital in Belfast for urethral discharge, rheumatism and eye trouble for 6 months before admission; there was no evidence to show whether gonococci had been found in the secretions.

On admission of patient the mouth was in a very septic condition and there was a slight mucopurulent urethral discharge, smears showing a fair number of pus cells and epithelial cells, but no organisms were seen; cultures yielded a few colonies of *Staph. albus*. The right shoulder and left ankle joints were acutely inflamed and there was a bilateral purulent conjunctivitis; smears from both eyes were also negative for gonococci. Typical parakeratotic nodules were present on the soles of both feet and there was a marked parakeratosis, which consisted of heaped-up scales, on the glans penis and mucous membrane of the prepuce, but no parakeratotic nodules. Patient was not circumcised. Anterior urethroscopy showed well-marked areas of soft infiltration. Smears after prostatic massage showed a fair number of pus cells but no organisms, and cultures yielded a profuse growth of *Staph. albus*. The Wassermann reaction was negative; the G.C.F.T. (gonococcal complement fixation test) was not carried out. The temperature during the first 3 weeks ranged between 99° and 100° F. Patient was discharged cured (16.9.29), but was readmitted 6 months later with a profuse non-gonococcal urethral discharge, conjunctivitis, acute arthritis of right knee and small patches of parakeratosis on glans penis; he remained in hospital for a further 2 months.

Treatment consisted of urethro-vesical irrigations, vaccines, and radiant heat and 5 per cent iodine applied to the joints affected.

Case 2

H. R., a picture-frame-maker aged 45 years, was admitted (3.4.33) with gonococcal urethritis of 3 months' duration, polyarthritis and keratodermia blennorrhagica. There was a previous history of gonorrhoea in 1917 and acute rheumatism in 1923.

At the time of the patient's admission the teeth and gums were in a very septic condition. A smear of the urethral discharge showed Gram negative diplococci, intracellular in position, but cultures yielded only a profuse growth of diphtheroids. The Wassermann reaction was negative. There was an acute arthritis of the small joints of the hands and feet; both knees and right ankle showed, to a marked degree, the presence of osteoarthritis, confirmed by skiagrams. On admission there were many well-developed parakeratotic nodules on the sole of the left foot and to a lesser extent on the right; there was also a parakeratosis on the glans penis. All skin lesions had entirely disappeared before discharge from hospital. (It was not noted whether circumcision had been carried out.) No further lesions appeared during treatment. The temperature was normal most of the time during the period of observation and only once rose to 99·8° F. The pulse rate ranged between 90 and 120 for 2 months and subsequently was never above 90; no cardiac lesion could be detected. Blood count (28.4.33) showed: red blood cells 4,100,000 per cubic millimetre; haemoglobin 68 per cent; colour index 0·84; white cells 14,000: polymorphs 71·5 per cent, eosinophils 2 per cent, basophils 1 per cent, lymphocytes 22·5 per cent, large mononuclears 3 per cent. The Wassermann reaction was negative.

Treatment consisted of urethro-vesical irrigation, vaccines, radiant heat and massage. Progress was slow and patient remained in hospital for 5 months.

Case 3

J. G., a civil servant aged 27 years, admitted (9.10.34) with gonococcal urethritis, polyarthritis, bilateral conjunctivitis and keratodermia blennorrhagica. Previous history of uncomplicated gonorrhoea in 1929. The present attack of urethritis developed 3 weeks before admission and conjunctivitis and arthritis 3 weeks later. On admission there was a mucopurulent urethral discharge containing gonococci. The Wassermann and Kahn reactions were negative and the G.C.F.T. was positive. Blood count: red cells 5,520,000; haemoglobin 80 per cent; colour index 0·72; white cells 14,000: polymorphs 82 per cent, eosinophils 2 per cent, basophils 2 per cent, lymphocytes 9 per cent, monocytes 5 per cent. Smears from the eyes (bilateral conjunctivitis) were negative for gonococci. There was an acute arthritis of both knees. Early vesicular lesions of keratodermia blennorrhagica were present on the soles of both feet, and on the sole of the left foot there was also one large bulla (see Plate A). The fluid aspirated from the lesions contained large numbers of epithelial cells; no pus cells or organisms were seen and cultures remained sterile. All lesions developed into hard parakeratotic nodules. The patient was acutely ill, with a swinging temperature, and a week after admission the left wrist became involved, but no further lesions of keratodermia blennorrhagica appeared. Blood cultures were sterile.

Treatment consisted of urethro-vesical irrigations, vaccines (gonococci and secondary organisms) at 5-day intervals, also radiant heat and 5 per cent iodine to the joints affected. A rise in fever followed each injection of vaccine, with beneficial effects. Patient was discharged cured 3 months after admission.

Case 4

H. A., a porter aged 30 years, was admitted (10.7.35) with gonococcal arthritis, polyarthritis, bilateral conjunctivitis, tachycardia and keratodermia blennorrhagica. There was a previous history of an attack of gonorrhoea with polyarthritis in 1931.

Urethral discharge was first noticed 5 weeks before admission. Eye trouble and arthritis developed 3 weeks later. On admission there was a slight urethral discharge containing pus cells and gonococci. The Wassermann and Kahn tests were negative and the G.C.F.T. was positive (+). Blood count: haemoglobin 78 per cent; red cells 4,810,000 per cubic millimetre; colour index 0·81; white cells 18,500: polymorphs 58 per cent, lymphocytes 35 per cent, eosinophils 1 per cent, basophils 1 per cent, monocytes 5 per cent. There was an acute arthritis of both knees and the left ankle and bilateral conjunctivitis; smears from the eyes were negative for gonococci. There were typical parakeratotic nodules on the soles of both feet and 2 nodules on the glans penis (the patient was circumcised). No further lesions developed. The patient was acutely ill. The temperature ranged between 100° and 103° F. for nearly 3 weeks; during the same period the pulse rate varied between 120 and 140. No cardiac lesion was detected. Blood cultures were sterile after 5 days' incubation.

Treatment consisted of urethro-vesical irrigations, vaccines (gonococci with secondary organisms), fever therapy induced by 5 intravenous injections of Dmelcos vaccine, and 5 per cent iodine and radiant heat to the joints affected. Rapid improvement followed fever therapy and the patient was discharged cured 2 months after admission.

Case 5

F. A. C., a porter aged 26 years, was admitted to St. Charles' Hospital (25.9.35) with gonococcal polyarthritis, bilateral iritis and keratodermia blennorrhagica. No previous history of venereal disease. Urethral discharge was first noticed 4 weeks before admission and was followed by iritis 3 weeks later; acute arthritis developed a few days before admission. At time of patient's admission the teeth and gums were in a very septic condition. Smears of the urethral discharge contained large numbers of gonococci, and cultures were also positive. The Wassermann and Kahn tests were both negative; the G.C.F.T. was doubtful (±) during the first 3 weeks in hospital and subsequently became positive (+); the reaction may have been evoked by injections of vaccine. There was an acute arthritis of both knees and the left ankle and an acute bilateral iritis. A parakeratosis, which extended partly on to the mucous membrane of the prepuce, covered the glans penis; it did not contain parakeratotic nodules. (Patient not circumcised.) Superficial vesicles, which soon became pustules, appeared on the soles of both feet one week after admission and within 48 hours had developed into parakeratotic nodules. A rupia-like lesion appeared over the crest of left tibia a few days later. Fluid and scraping from vesicles and pustules consisted entirely of epithelial cells and no organisms or pus cells were seen; cultures were sterile. The temperature during the first 3 weeks ranged between 99° and 101° F.; blood cultures were sterile. Skiagrams of joints showed no abnormalities.

Treatment consisted of urethro-vesical irrigations, vaccines (gonococci with secondary organisms) every 5 days, radiant heat and 5 per cent iodine twice daily to the joints affected, also guttae atropinae, spoon-bathing and dark glasses for the iritis. General reactions followed intramuscular injections of vaccine, with beneficial effects, and the patient was discharged cured after 6 weeks in hospital. All skin lesions had entirely disappeared and there was no scarring.

Case 6

F. W., a painter aged 51 years, was admitted to St. Charles' Hospital (5.10.35) with gonococcal polyarthritis and keratodermia blennorrhagica. Previous history of gonorrhoea with polyarthritis in 1915. Urethral discharge was first noticed one month before admission and an acute arthritis of both knees developed a week later. On admission of patient urethral smears were positive for gonococci and cultures yielded a mixed growth of gonococci and *Staph. albus;* Wassermann and Kahn tests were both negative and G.C.F.T. was strongly positive. The temperature ranged between 99° and 100° F. There was acute arthritis of both knees, the movements of the joints being limited to a marked degree and the least movement causing agonizing pain; skiagram showed no bony changes. Vesicular, pustular and nodular lesions of keratodermia blennorrhagica were present on the soles of both feet, extending on the inner sides to the internal malleolus of the tibia; no further crops appeared. Serum aspirated from vesicles and pustules consisted of epithelial cells only and cultures were sterile. An excised vesicle gave the typical histological picture of keratodermia blennorrhagica; no organisms were seen in sections; blood cultures were sterile.

Treatment consisted of urethro-vesical irrigations, vaccine (gonococci and secondary organisms) at 5-day intervals, and radiant heat and 5 per cent iodine in spirit twice daily to the knees. Sharp general reactions, which followed each intramuscular injection of vaccine, had a beneficial effect; the patient was discharged cured one month after admission.

Case 7

C. R. W., a bookmaker's clerk aged 40 years, was admitted (12.12.35) with non-gonococcal urethritis, polyarthritis, bursitis and keratodermia blennorrhagica.

There was a previous history of gonorrhoea and polyarthritis in 1920, and urethral discharge was noticed one month before admission. The patient treated himself with "injections" of potassium permanganate, and 2 days before admission pains developed in several joints. On admission there was a clear mucoid secretion at the external urinary

meatus and smears contained only a few pus cells ; no organisms were seen and cultures were sterile. Smears and cultures after prostato-vesicular massage were also negative for gonococci. The Wassermann and Kahn tests were negative and G.C.F.T. was strongly positive. There was an acute arthritis of the left knee and both elbows, and the right olecranon bursa was inflamed and distended ; skiagram of joints showed no bony changes. There was a parakeratotic balanitis (patient was not circumcised) and there were 2 limpet-like parakeratotic lesions on the scalp. No further lesions developed during the period of observation. There was a swinging temperature for 3 weeks. Blood cultures were sterile.

Treatment consisted of urethro-vesical irrigations, vaccines, and radiant heat and 5 per cent iodine to the joints affected. The non-specific protein shock effect of the weekly injection of vaccine was the determining factor in effecting a cure (18.2.36).

Case 8

W. H., a clerk aged 37 years, was admitted to hospital (23.4.36) with gonococcal polyarthritis, left conjunctivitis and keratodermia blennorrhagica. Previous history of gonorrhoea with epididymitis and arthritis in 1926. The present attack of gonorrhoea began 19 days before admission and after 14 days was complicated by acute iritis and 2 days later by acute arthritis. On admission of patient the mouth was in a very septic condition and there were vesicles and small superficial ulcers on the buccal mucous membrane and hard palate. Urethral smears and cultures were positive for gonococci. The left Cowper's gland was palpable and smears after massage contained gonococci. The Wassermann and Kahn tests and G.C.F.T. were negative, the G.C.F.T. remaining negative throughout the period of observation in spite of injections of gonococcal vaccines. Blood count : haemoglobin 80 per cent ; red blood cells 4,500,000 ; colour index 0·88 ; white cells 12,000 : polymorphs 64 per cent, lymphocytes 29 per cent, eosinophils 1 per cent, monocytes 6 per cent. (Slight anisocytosis was noted.) There was an acute arthritis of both mid-tarsal joints, and early lesions of keratodermia blennorrhagica (vesicles and pustules) were present on the soles of both feet. Plate B shows lesions on right foot.) Smears from these early lesions showed numerous epithelial cells but no pus cells or organisms (including tubercle bacilli) and cultures were sterile ; one of many culture tubes gave a scanty growth of diphtheroids, which was considered to be a contamination. One lesion was excised and sepsis of the sole of the foot occurred after the operation. A further crop of vesicles appeared on the soles of the feet one week after admission and at the same time the left knee became acutely inflamed. Within 3 days the vesicles had developed into parakeratotic nodules (see Plate C, showing lesions on right foot), and on the same date multiple discrete and soft parakeratotic areas were noted on the mucous membrane of the prepuce. (The patient was not circumcised.) The areas remained discrete and removal of scabs revealed an oozing surface (see Plate G). Large and small soft limpet-like hyperkeratotic lesions appeared on the scalp 5 weeks later (see Plate D). The disease ran a septicaemic course, the temperature ranging between 99·4° and 102° F. ; blood cultures (4.6.36) were sterile.

Treatment consisted of urethro-vesical irrigations, vaccine, radiant heat and 5 per cent iodine in spirit to the joints affected, spoon-bathing to the left eye and atropine ointment 1 per cent. Fever therapy was induced with intravenous injections of Dmelcos vaccine (14.7.36) ; after 2 injections of 0·25 and 0·5 cubic centimetres the temperature returned to normal and the patient made a rapid recovery ; he was discharged 22 days later.

Case 9

S. M., a clerk aged 32 years, was admitted (17.10.36) with gonococcal polyarthritis and keratodermia blennorrhagica. No previous history of venereal disease. Contracted gonorrhoea 4 weeks before admission and was treated with anterior urethral wash-outs at Whitechapel Clinic. Arthritis developed 7 days after he contracted the disease. On examination the mouth was in a very septic condition. There was a pin-point urethral meatus ; urethral smears were negative for gonococci and cultures yielded a few colonies of *Staph. albus*. The Wassermann and Kahn reactions and G.C.F.T. were negative, the latter not becoming positive until the sixth week after admission, when it was possibly evoked by the weekly administration of a vaccine. Smears and cultures after prostatic massage were also negative for gonococci. At time of admission there were many well-marked parakeratotic nodules on the soles of both feet and over the lower quarter of right and left tibia ; no further lesions developed ; all nodules had fallen off before date of discharge and there was no scarring. There was acute synovitis of both knees with marked wasting of the muscles above and below the joints affected ; skiagram of joints showed no bony changes. The temperature remained just above normal for 3 weeks and never registered higher than 100° F.

Treatment consisted of urethro-vesical irrigations, vaccines (gonococci with secondary organisms), radiant heat to the joints affected and massage. Discharged to duty 10.12.36.

Case 10

C. R., a labourer aged 33 years, was admitted to St. Charles' Hospital (15.6.37) with gonococcal urethritis (contracted 3 days previously), acute polyarthritis and bilateral conjunctivitis ; keratodermia blennorrhagica, endocarditis and pericarditis developed later. There was a previous history of an attack of uncomplicated gonorrhoea in 1930.

A purulent conjunctivitis (metastatic) developed 24 hours after the appearance of the urethral discharge ; 48 hours later there was an acute arthritis of the right metatarso-phalangeal joint of the great toe and 24 hours later the left ankle became involved. At time of admission smears of the urethral discharge contained large numbers of gonococci

and cultures yielded a mixed growth of gonococci and *Staph. albus*. Repeated smears from both eyes contained many pus cells, but no organisms were seen and cultures were sterile. The Wassermannn and Kahn reactions and G.C.F.T. were negative. Other joints (left wrist and both knees) became involved (22.6.37), and typical early lesions of keratodermia blennorrhagica appeared on the soles of both feet (13.7.37), rapidly developing into pustules and typical parakeratotic nodules. A few days later similar indurated and discrete lesions were noted on the glans penis in the region of the coronal sulcus (see Plate E); there were also two areas of soft (not nodular) heaped-up scales (circinate balanitis) on the mucous membrane of the prepuce and extending forwards to the edge of the glans. (The patient was not circumcised but the prepuce did not cover the glans.) Removal of these heaped-up scales exposed a weeping surface. Repeated smears from the early lesions on the soles of the feet showed only epithelial cells and no pus cells or organisms, and cultures were sterile. Further crops of lesions, which subsequently developed into typical keratotic nodules, appeared (24.7.37) on the extensor aspects of both legs and on the inner side of the left thigh; there were also 2 lesions in the region of the umbilicus.

The disease ran a septicaemic course, the temperature ranging between 99° and 101·6° F. with a rapid pulse (120). Blood cultures (9.8.37) were sterile after 10 days' incubation. A presystolic thrill (9.8.37) and pericarditis (16.8.37) developed. There was a marked laxity of the ligaments of the affected joints. There was subluxation backwards of the right tibia, also displacement outwards and internal rotation. This compound subluxation of the joint was completely reducible by manipulation and no pain was experienced by the patient. Triple extension was applied and a perfect result was obtained; on patient's discharge all joints were normal.

Routine treatment consisted of urethro-vesical irrigations, weekly vaccine (gonococci with secondary organisms), 5 per cent iodine in spirit and radiant heat twice daily to the joints affected. Eye treatment consisted of repeated swabbing with warm solution of mercury perchloride, 1 in 8,000, silver nitrate, 1 per cent twice daily, mercuric oxide ointment, and 2 per cent atropine at night. Fever therapy, by means of intravenous injection of 0·5 cubic centimetres of Dmelcos vaccine, was given on 20.7.37 and repeated at 48-hour intervals until 2 further injections of 1 cubic centimetre and 1·5 cubic centimetres had been given. There was considerable improvement, but the patient refused further injections. Sulphanilamide, 1 gramme thrice daily, was prescribed (9.8.37) with excellent results. Convalescence was slow and patient was not discharged until 5½ months after admission.

The patient was subsequently admitted under my care (12 months later) with a re-infection, which reacted rapidly to sulphapyridine. It is interesting to note that when he was admitted there were two rupia-like lesions on the glans penis. The Wassermann and Kahn reactions and G.C.F.T. were negative.

Case 11

A. T. P., a builder aged 34 years, was admitted to St. Charles' Hospital (24.7.37) with non-gonococcal urethritis, polyarthritis, painful heels and keratodermia blennorrhagica.

I had treated this patient 5 years previously for a severe attack of gonorrhoea complicated by acute polyarthritis, metastatic conjunctivitis, acute myalgia of right and left trapezius muscles and painful heels. There were then no skin lesions and the Wassermann and Kahn tests and G.C.F.T. (carried out on 4 occasions) were negative. During convalescence the patient had been treated for lobar pneumonia. The painful heels (due to large subcalcanean spurs) continued to be troublesome and, as they failed to be benefited by radiant heat, sorbo rubber pads and injections of oily nupercaine, excision of both spurs was carried out and the immediate result had been excellent.

Condition on his admission on the second occasion (24.7.37) showed a profuse urethral discharge, smears containing many pus cells but no organisms, and cultures yielding a scanty growth of *Staph. albus*. Smears and cultures after prostato-vesicular massage were also negative for gonococci. The Wassermann and Kahn tests and G.C.F.T. were negative. There was a subacute arthritis of both ankles and acute tenderness of both heels. X-ray examination showed that 2 large subcalcanean spurs had reappeared during the 5 years' interval following the operation for excision. Parakeratotic nodules were present on the soles of both feet, being first noticed by patient a fortnight before admission. The temperature was normal during the 6 weeks' stay in hospital and no fresh skin lesions appeared. The condition reacted rapidly to urethro-vesical irrigations, vaccines and radiant heat. The keratotic nodules had all fallen off before patient's discharge and there was no scarring.

Case 12

J. J., a cook aged 37 years, was admitted (26.10.37) with gonococcal urethritis, polyarthritis and keratodermia blennorrhagica. Previous history of gonorrhoea 2 and 5 years before the present illness, the last attack with polyarthritis; reinfected 3 weeks before admission. On admission there was a purulent gonococcal urethral discharge. The Wassermann and Kahn reactions and G.C.F.T. were all negative. Blood count: red cells 5,200,000; haemoglobin 90 per cent; colour index 0·86; white cells 12,000 per cubic millimetre. There was an acute arthritis of left shoulder and right knee. Parakeratotic nodules were present on the soles of both feet, but no further lesions developed during the period of observation, in spite of the fact that an acute exacerbation of the arthritis, with involvement of several interphalangeal joints of the right hand, occurred 14 days after admission. The temperature ranged between 99° and 101° F. Blood cultures were sterile after 5 days' incubation.

Treatment consisted of urethro-vesical irrigations, vaccines, and radiant heat and 5 per cent iodine to the joints affected. The condition did not improve until fever therapy was induced by the intravenous injection of Dmelcos vaccine. Four injections were given and an excellent result followed. Patient was discharged cured, 20.1.38.

Case 13

E. D. E., a railway porter aged 52 years, was admitted to St. Charles' Hospital on 16.4.38 with a diagnosis of gonococcal polyarthritis ; keratodermia blennorrhagica developed later. There was a previous history of gonorrhoea in 1916 and 1927, the latter attack being complicated by an acute polyarthritis.

There was no history of a recent infection and the patient stated that he did not notice a urethral discharge until the onset of the arthritis. He was admitted to a London hospital (8.4.38) and the right wrist, the only joint involved at the time, was incised ; gonococci were found in the synovial fluid. At time of admission (16.4.38) the mouth was in a very septic condition and there was an acute arthritis of right wrist, both knees and ankles and first right metacarpophalangeal joint ; there was also an associated inflammation of the bursa over the right gluteus medius muscle. Gonococci were present in the urethral discharge and the G.C.F.T. was doubtful and subsequently positive, which change may have been provoked by weekly injections of a vaccine. Wassermann and Kahn tests were negative. Urethroscopy revealed a stricture large enough to admit an F_2 bougie.

Sharply defined parakeratotic lesions developed in the scalp and back (3.5.38) during a course of sulphanilamide, and a fortnight later (during a course of sulphapyridine) vesicles on the soles of both feet. At the same time there was an acute exacerbation of the arthritis and a small localized periostitis over the lower third of the right tibia. The fluid aspirated from the vesicles contained a large number of epithelial cells but neither pus cells nor organisms, and cultures were sterile. Vesicles developed into pustules and typical parakeratotic nodules. All the lesions had completely disappeared before patient's discharge from hospital 3 months after admission and there was no scarring. Blood cultures were sterile. The temperature varied between 100° and 101° F. when the skin lesions appeared ; x-ray examination of joints showed no bony changes.

Treatment consisted of chemotherapy, urethro-vesical irrigations with potassium permanganate, 1 in 8,000, radiant heat baths twice daily to the joints affected, weekly intramuscular injections of a mixed vaccine, and urethral dilatations. No local treatment was prescribed for the skin lesions. Although it was not realized at the time, this was a typical case of drug resistance. At the present day fever therapy would be the treatment of choice.

Case 14

D. L. R., a traveller aged 36 years, was admitted to St. Charles' Hospital (20.6.38) with gonococcal polyarthritis, right iritis and keratodermia blennorrhagica. Gonorrhoea, contracted 7 weeks before admission, was followed 4 weeks later by acute arthritis ; iritis developed 1 week before admission. There was no previous history of venereal disease. At St. Paul's Hospital, before his admission to St. Charles' Hospital, gonococci were found in the discharge, but we failed to find them in smears and cultures of the discharge, urine (which was muddy in all glasses) or prostatic secretion. The Wassermann and Kahn reactions and G.C.F.T. were carried out at weekly intervals and remained negative throughout the period of observation. Blood count : red cells 4,500,000 per cubic millimetre ; haemoglobin 64 per cent ; colour index 0·71 ; white cells 17,000 : polymorphs 73 per cent, lymphocytes 22 per cent, monocytes 3·5 per cent and eosinophils 1·5 per cent. The mouth was in good condition. There was an acute arthritis of both knees, with restricted movements, also an acute iritis of the right eye. Parakeratotic nodules, hard and discrete, were present on the soles of both feet ; there were several soft parakeratotic areas on the glans penis and on the mucous membrane of prepuce ; they subsequently coalesced to form a large limpet-like scab ; it eventually came away in one large mass, one month after admission, and left a dry surface on the glans penis. One nodule under the nail of the right great toe caused a good deal of pain and was excised, without any local anaesthesia being required. The temperature, 100·2° F. at time of admission, returned to normal after 4 days' treatment.

Before admission this patient had been given a course of sulphanilamide with sub-effective dosage, and on admission he received a 14 days' course of sulphapyridine, which I was testing before the drug was put on the market. Combined with urethro-vesical irrigations and vaccines, it had a beneficial effect, as did the radiant heat and 5 per cent iodine in spirit which were used for the affected joints. Iritis was treated by means of spoon-bathing with warm boracic lotion, and an ointment containing atropine 1 per cent and argyrol 10 per cent. Patient was discharged cured, 30.7.38.

Case 15

G. T. C. D., a cabinet-maker aged 24 years, was admitted (23.8.38) with non-gonococcal urethritis, polyarthritis, bilateral conjunctivitis and keratodermia blennorrhagica.

The history showed that he was treated at home by his own doctor for rheumatism and a discharge, 6 months before admission. The urethral discharge had persisted, and 4 days before his admission there was an acute exacerbation of the rheumatism and both eyes became painful. On admission there was a slight urethral discharge containing pus cells, but no gonococci were seen and cultures yielded a pure growth of *Staph. albus*. Smears and

cultures after prostato-vesicular massage were also negative for gonococci. Wassermann and Kahn reactions were negative and the G.C.F.T. was positive. Blood count: red cells 5,700,000; haemoglobin 90 per cent; colour index 0·79; white cells 15,000: polymorphs 73 per cent, basophils 1 per cent, lymphocytes 15 per cent, monocytes 11 per cent. There was an acute arthritis of both ankles and the left knee, also a bilateral purulent conjunctivitis and left iritis. Smears from the eyes showed large numbers of pus cells, but there were no organisms; cultures gave a pure growth of *Staph. albus*. Six typical parakeratotic nodules were visible on the glans penis only (patient was circumcised); they remained discrete and eventually fell off; no further lesions developed. The temperature during the first fortnight ranged between 98·2° and 100° F., but a rise up to 102·6° F. followed each injection of a mixed vaccine.

Treatment consisted of urethro-vesical irrigations, sulphapyridine, vaccines, and radiant heat and 5 per cent iodine in spirit to the joints affected. The eyes were treated with lotio hydrargyri perchloridum, 1 in 8,000, protargol, 10 per cent, and atropine ointment, 1 per cent. The patient was discharged cured, 18.10.38.

Case 16

A. S., a cook aged 28 years, was admitted under my care (11.4.39) with gonococcal polyarthritis, bilateral conjunctivitis and keratodermia blennorrhagica. No previous history of venereal disease. Urethral discharge was first noticed by patient 6 weeks before admission; acute arthritis (left knee) and conjunctivitis developed 2 days later. He was then admitted to a London hospital, where the urethral infection was overlooked, but a subsequent examination of fluid aspirated from the knee joint was positive for gonococci in both smears and cultures. Three weeks' treatment with sulphapyridine (4 grammes daily) was prescribed before the patient was transferred to me. At time of admission smears of the urethral discharge contained large numbers of pus cells and Gram positive cocci, and cultures yielded a mixed growth of *Staph. albus* and coliform bacilli; smears after prostatic massage were also negative for gonococci. The urine was muddy in all glasses. Wassermann and Kahn reactions were negative; the G.C.F.T., doubtful at time of admission, became strongly positive after 2 vaccine injections. Blood count: red cells 4,580,000; haemoglobin 76 per cent; colour index 0·84; white cells 11,000: polymorphs 71 per cent, lymphocytes 20 per cent, eosinophils 3 per cent, monocytes 6 per cent. There was an acute arthritis of left knee and metatarsophalangeal joints of left foot. Four typical lesions (parakeratotic nodules) of keratodermia blennorrhagica were present on sole of right foot only; they, as is usual, were symptomless and had not previously been diagnosed. Within 6 weeks all the nodules had fallen off, leaving a smooth unscarred skin. The temperature ranged between 99° and 100° F. for 3 weeks and then returned to normal.

Treatment consisted of urethro-vesical irrigations, intramuscular injections of vaccine (gonococci with secondary organisms) and 5 per cent iodine and radiant heat twice daily to the joints affected. A marked general non-specific reaction with fever occurred after each vaccine injection; the urine cleared rapidly and the acute condition in the joints subsided. Patient was not discharged from hospital until 15.7.39, as the knee joint had been splinted for one month before he was transferred to us. Limitation of movement was marked and treatment, which included massage and active and passive movement, was necessary.

Case 17

H. H., a salesman aged 31 years, was admitted to hospital (25.7.39) with gonococcal arthritis, tenosynovitis and keratodermia blennorrhagica. No previous history of venereal disease. Gonorrhoea had been contracted 14 days before his admission and arthritis and tenosynovitis developed 4 days later. At time of admission urethral smears were positive for gonococci. Wassermann and Kahn reactions were negative and the G.C.F.T. was strongly positive; mouth was in good condition. There was an acute arthritis of the left wrist and tenosynovitis of the extensor tendon of the right index finger; 6 days later (during a course of sulphapyridine) arthritis extended to third right metatarsophalangeal joint. On the glans penis there were 5 typical keratotic nodules of keratodermia blennorrhagica, which were painless and had not been previously diagnosed. (The patient was circumcised.) The lesions remained discrete, did not coalesce to form a parakeratotic balanitis and subsequently fell off 4 weeks later. X-ray examination of joints affected showed no abnormality.

The patient reacted well to vaccines (gonococci with secondary organisms) and urethro-vesical irrigation; a general reaction with rise in fever up to 100° F. followed each injection of the vaccine. Chemotherapy was unsuccessful and was omitted after 5 days' trial, when a generalized scarlatiniform eruption developed. Patient discharged cured 5 weeks after admission.

Case 18

Male, aged 35 years, admitted (25.9.44) with non-gonococcal urethritis, polyarthritis, bilateral metastatic conjunctivitis. Lesions of keratodermia blennorrhagica were subsequently provoked by exposure to radiant heat and the application of ichthyol ointment, 10 per cent. Previous history showed that in 1934 the patient had suffered from gonorrhoea and polyarthritis.

On admission there was a profuse urethral discharge (first noticed 12 days after marital intercourse and 10 days before admission) containing large numbers of pus cells, epithelial cells and a few Gram positive organisms; gonococci were not found, and this was also the case in smears and cultures after prostato-vesicular massage; cultures yielded a few colonies

of *Staph. albus*. There was a bilateral purulent conjunctivitis, smears showing large numbers of pus cells ; no organisms were seen and cultures were sterile. A subsequent smear after the commencement of treatment showed Gram negative and Gram positive bacilli. Inclusion bodies were seen in the epithelial cells of both the urethral discharge and the conjunctival secretion. The left knee joint was acutely inflamed and an acute arthritis of right knee, both wrists and third right metatarsophalangeal joint subsequently developed. Wassermann and Kahn reactions and G.C.F.T. were negative ; the Frei test was also negative. Erythrocyte sedimentation rate throughout the period of observation was 57-60 millimetres in 1 hour. The temperature during the first month varied between 99° and 101° F. Urethroscopy did not reveal the presence of a granular urethritis. On admission the man was suffering from scabies, and there was a large hyperkeratotic limpet-like lesion surrounding the right nipple, removal of which left a weeping surface. The lesion subsequently re-formed but to a lesser extent. In the first place there were no parakeratotic nodules on the soles of the feet, but two small lesions were subsequently provoked on the sole of the left foot by radiant heat treatment and the application of 10 per cent ichthyol in vaseline. Unfortunately the lesions were not discovered until they had developed into parakeratotic nodules, and the opportunity to examine early lesions for inclusion bodies was thus lost. The nodules were removed, however, but microscopic examination of the scales showed only doubtful inclusion bodies.

Treatment consisted of sulphathiazole, urethro-vesical irrigations and fever therapy, silver nitrate, 1 per cent, and 1 per cent atropine ointment for the eyes, and radiant heat and 5 per cent iodine to the joints affected. Chemotherapy and 100,000 units of penicillin (given to the patient before admission) had had no effect on the disease. Marked improvement followed 2 intravenous injections of 50 and of 75 millions anti-typhoid-paratyphoid vaccine ; the patient refused further injections. Discharged to convalescent home, 17.11.44.

Case 19

H. J., aged 39 years, with non-gonococcal urethritis, polyarthritis, conjunctivitis, iritis and keratodermia blennorrhagica.

There was a previous history of non-gonococcal urethritis, conjunctivitis and polyarthritis in 1941 and 1943. On both occasions the G.C.F.T. was negative and fever therapy induced by T.A.B. vaccine effected apparent cure. No previous history of gonorrhoea.

Urethral discharge and dysuria were first noted (22.3.45) 4 days after sexual intercourse. He had had intercourse with the same woman during the preceding 6 months, but on all previous occasions he had used a condom. Pains in joints were not noted until 14 days after the appearance of the urethral discharge ; 2 days later there was a bilateral conjunctivitis.

Smears of the urethral discharge contained many pus cells and epithelial cells. Inclusion bodies were found in the epithelial cells of the urethral discharge and conjunctival secretion ; cultures were sterile. Wassermann and Kahn reactions and G.C.F.T. were negative. Erythrocyte sedimentation rate was 55. The temperature ranged between 99° and 102° F. The arthralgia developed into an acute arthritis of knees and ankles and of the interphalangeal joints of both hands, and a few days later there was a right iritis. X-ray examination of joints showed no bony changes.

A parakeratotic balanitis (see Plate F) was noted on 24.4.45, and typical vesicles, which developed into pustules and parakeratotic nodules, appeared a few days later on the soles of both feet. Smears from the lesions showed large numbers of elementary bodies ; cultures for pleuropneumonia-like organisms were unsuccessful. The patient is now convalescent, after treatment with 5 sessions of fever, induced by T.A.B. vaccine.

Case 20

J. R., aged 36 years, with non-gonococcal urethritis, bilateral conjunctivitis, polyarthritis and keratodermia blennorrhagica. Urethral discharge first noticed (6.4.45) 4 weeks after sexual intercourse ; no previous history of venereal disease. Bilateral conjunctivitis developed on 21.4.45 and polyarthritis on 23.4.45. Before seeing me (21.4.45) he had received a 4-days' course of sulphathiazole, 1 gramme 4-hourly.

Smears of the purulent urethral discharge contained no organisms and cultures were sterile ; cultures for pleuropneumonia-like organisms were also unsuccessful ; inclusion bodies were seen in the cytoplasm of the epithelial cells of both the urethral discharge and the conjunctival secretion. The urine was muddy in all glasses. The Wassermann and Kahn reactions and G.C.F.T. were negative. There was an acute arthritis of both mid-tarsal joints and the metatarsophalangeal joint of the right great toe ; there was also a periostitis of the proximal phalanx of the right index finger.

A solitary vesicle, which developed into a pustule and parakeratotic nodule, appeared on the edge of the glans penis (4.5.45). Large numbers of elementary bodies were seen in smears made from the contents of the pustule. A week later similar lesions developed on the sole of the right foot and on the skin of the lower lip ; at the same time a limpet-like parakeratotic patch surrounded the external urinary meatus ; the lesions on the foot and mouth also contained large numbers of elementary bodies. It is interesting to note that the patient's temperature has remained normal throughout and that there has been no rise even when the vesicles appeared.

Fever has been induced by T.A.B. vaccine, but progress is slow ; injections of gold salts (myocrisin) are being tried, in spite of the fact that pleuropneumonia-like organisms have not so far been isolated. Administration of one million units of penicillin has had no effect.

Summary

(1) A review is given of the skin lesions which are seen in gonorrhoea ; they may be local or systemic.

(2) Among the systemic manifestations a detailed description is given of the clinical findings in 20 cases of keratodermia blennorrhagica.

(3) Attempts at isolating gonococci and other organisms from the lesions were unsuccessful in all cases.

(4) It is suggested that keratodermia blennorrhagica is a skin manifestation of non-gonococcal urethritis, probably due to a virus and occurring alone or in association with gonorrhoea ; the elementary bodies found may be the granular phase in the development of pleuropneumonia-like organisms.

(5) Fever therapy is considered to be the treatment of choice.

(6) Attention is drawn to the similarity of the histological findings in keratodermia blennorrhagica and in psoriasis.

My thanks are due to Dr. Bauer and Mr. Dossett of the Wellcome Research Institution for carrying out laboratory investigations, and to Major Haber for translations of the German articles to which reference is made.

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DISCUSSION ON THE PRECEDING PAPER

Brig. T. E. Osmond (the President) said that Dr. Harkness's paper had been very interesting and decidedly provocative.

Dr. **Hanschell** congratulated Dr. Harkness on the interesting and valuable information which he had put forward. It was a matter of great interest to learn that in the lesions which they had all seen, in which a sinus was discharging gonococci, a biopsy would show the sub-epithelial tissue to be actually infected with the gonococci. He had not looked for inclusion bodies in residual urethritis, but he agreed with Dr. Harkness that clinically the condition cleared up and was apparently cured by fever therapy. As to the keratodermia lesions, he had observed them in 1 out of 10,000 cases and, looking at the lesions which Dr. Harkness had presented so vividly, he thought that some of the penile lesions which he had allowed to pass, thinking that they were due to mechanical injury, were keratodermia lesions. He had seen the heaped-up, rather sodden epithelium; in places it seemed to be rubbed off. He had however concluded that the patient had been too vigorous and unwise in treating himself with antiseptics and the other remedies with which patients scrubbed themselves.

Lt.-col. **A. J. King** said that his first reaction to the title of this paper had been that it was a very limited subject, but Dr. Harkness had shown how wrong was such an assumption. He had given so much information that his hearers would be glad to have the opportunity of studying the paper at leisure.

There were one or two points of special interest. Lt.-col. King was surprised that keratodermia blennorrhagica was regarded as being such a rarity. Perhaps he was fortunate at Westbury in having a specially selected group of cases, but there was rarely a time in the wards when 2 or 3 cases of this condition could not be seen. Part of the general opinion as to the rarity of these cases was due to a fact which Dr. Harkness had emphasized, namely that these lesions were sometimes inconspicuous and that unless special search was made for them they were sometimes missed. They were present on the soles of the feet and might not grow to any size.

The condition which Dr. Harkness had described as circinate balanitis was perhaps the commonest manifestation of this particular syndrome, and was one which often was either missed or not interpreted in association with the general condition. It was a condition which he had seen fairly often. One of its characteristics was that, unlike the lesions on the skin, it often preceded the arthritis; in fact, more than once it had been possible to foretell the onset of metastatic lesions by noticing the presence of the balanitis.